
Handbook of PHARMACEUTICAL EXCIPIENTS

Third Edition

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Calcium Phosphate, Dibasic Anhydrous

1. Nonproprietary Names

BP: Calcium hydrogen phosphate
PhEur: Calcii hydrogenphosphas anhydricus
USP: Dibasic calcium phosphate
JP: Anhydrous dibasic calcium phosphate

2. Synonyms

A-TAB; calcium orthophosphate; calcium monohydrogen phosphate; dicalcium orthophosphate; *Di-Cafos AN*; E341; E540; *Anhydrous Emcompress*; phosphoric acid calcium salt (1:1); secondary calcium phosphate.

3. Chemical Name and CAS Registry Number

Dibasic calcium phosphate [7757-93-9]

4. Empirical Formula Molecular Weight

CaHPO_4 136.06

5. Structural Formula

CaHPO_4

6. Functional Category

Tablet and capsule diluent.

7. Applications in Pharmaceutical Formulation or Technology

Anhydrous dibasic calcium phosphate is used both as an excipient and as a source of calcium in nutritional supplements. It is used particularly in the nutritional/health food sectors. It is also used in pharmaceutical products because of its compaction properties, and the good-flow properties of the coarse-grade material. The predominant deformation mechanism of anhydrous dibasic calcium phosphate coarse-grade is brittle fracture and this reduces the strain-rate sensitivity of the material, thus allowing easier transition from the laboratory to production scale. However, unlike the dihydrate, anhydrous dibasic calcium phosphate when compacted at higher pressures can exhibit lamination and capping. This phenomenon can be observed when the material represents a substantial proportion of the formulation and is exacerbated by the use of deep concave tooling.⁽¹⁾ This phenomenon also appears to be independent of rate of compaction.

Anhydrous dibasic calcium phosphate is abrasive and a lubricant is required for tableting, for example 1% magnesium stearate or 1% sodium stearyl fumarate.

Two particle-size grades of anhydrous dibasic calcium phosphate are used in the pharmaceutical industry. Milled material is typically used in wet-granulated or roller-compacted formulations. The 'unmilled' or coarse-grade material is typically used in direct-compression formulations.

Anhydrous dibasic calcium phosphate is nonhygroscopic and stable at room temperature. It does not hydrate to form the dihydrate.⁽²⁾

Anhydrous dibasic calcium phosphate is used in toothpaste and dentifrice formulations for its abrasive properties.

8. Description

Anhydrous dibasic calcium phosphate is a white odorless, tasteless powder or crystalline solid. It occurs as triclinic crystals.

9. Pharmacopeial Specifications

Test	JP	PhEur	USP
Identification	+	+	+
Characters	+	—	—
Description and solubility	—	+	+
Loss on ignition	—	—	6.6-8.5%
Loss on drying	—	—	≤ 1.0%
Acid insoluble substance	≤ 0.05%	—	≤ 0.2%
Heavy metals	≤ 31 ppm	≤ 40 ppm	≤ 0.003%
Lead	—	—	≤ 5 ppm ^(a)
Chloride	≤ 0.248%	≤ 330 ppm	≤ 0.25%
Fluoride	—	≤ 100 ppm	≤ 0.005%
Sulfate	≤ 0.200%	≤ 0.5%	≤ 0.5%
Carbonate	Absent	Absent	Absent
Barium	Absent	Absent	Absent
Arsenic	≤ 2 ppm	≤ 10 ppm	≤ 3 ppm
Monocalcium and tricalcium phosphates	—	14.0-15.5 ml	—
Organic volatile impurities	—	—	+
Iron	—	≤ 400 ppm	—
Assay (dried basis)	—	98.0-101.0%	98.0-105.0%

^(a) California Proposition 65 agreement: from April 1999 the limit for lead (Pb) in dibasic calcium phosphate dihydrate used in multimineral and/or multivitamin supplements will be ≤ 0.4 ppm based on current US RDA for elemental calcium. The limit for anhydrous dibasic calcium phosphate has not yet been agreed.

10. Typical properties

Acidity/alkalinity:

pH = 7.3 (20% slurry)

pH = 5.1 (20% slurry of A-TAB)

Compressibility: See Fig. 1.^(a)

Density: 2.89 g/cm³

Density (bulk): 0.78 g/cm³ for A-TAB

Density (tapped): 0.82 g/cm³ for A-TAB

Flowability: 18.9 g/s for A-TAB

Melting point: does not melt; decomposes at ≈ 425°C to form calcium pyrophosphate.

Moisture content: 0.1-0.187%,^(a) the anhydrous material only contains surface adsorbed moisture. It cannot be rehydrated to form the dihydrate.

Particle size distribution:

Average particle diameter

180 μm for A-TAB;

136 μm for *Emcompress Anhydrous*;

15 μm for powder.

Solubility: practically insoluble in ether, ethanol, and water; soluble, in dilute acids.

Specific surface area: 20-30 m²/g for A-TAB

^(a) *Handbook of Pharmaceutical Excipients*, First Edition.

Calcium Phosphate, Dibasic Dihydrate

Nonproprietary Names

P: Calcium hydrogen phosphate
D: Dibasic calcium phosphate
Eur: Calcii hydrogenophosphas dihydricus
SP: Dibasic calcium phosphate

Synonyms

Calphos; calcium hydrogen orthophosphate dihydrate; calcium monohydrogen phosphate dihydrate; *Calstar*; *Calipharm*; dibasic calcium orthophosphate; *Di-Cafos*; *DI-TAB*; E341; *Emcomess*; phosphoric acid calcium salt (1:1) dihydrate; secondary calcium phosphate.

Chemical Name and CAS Registry Number

Dibasic calcium phosphate dihydrate [7789-77-7]

Empirical Formula Molecular Weight

$\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ 172.09

Structural Formula

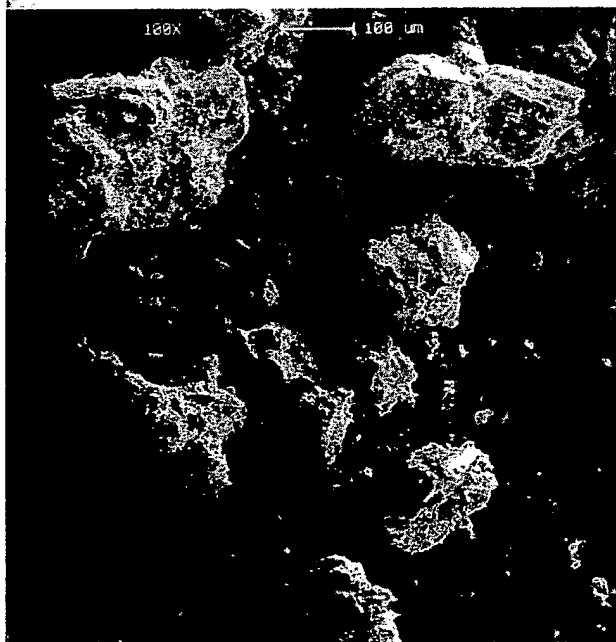
$\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$

Functional Category

Tablet and capsule diluent.

EM: 1

Excipient: Dibasic calcium phosphate dihydrate, coarse grade
Manufacturer: Penwest Pharmaceuticals
Lot: W28C
Magnification: 100x



7. Applications in Pharmaceutical Formulation or Technology

Dibasic calcium phosphate dihydrate is used both as an excipient and as a source of calcium in nutritional supplements. It is one of the more widely used materials, particularly in the nutritional/health food sectors. It is also used in pharmaceutical products because of its compaction properties, and the good-flow properties of the coarse-grade material. The predominant deformation mechanism of dibasic calcium phosphate coarse-grade is brittle fracture and this reduces the strain-rate sensitivity of the material, thus allowing easier transition from the laboratory to production scale. However, dibasic calcium phosphate dihydrate is abrasive and a lubricant is required for tableting, for example, about 1% magnesium stearate or about 1% sodium stearyl fumarate.

Two main particle-size grades of dibasic calcium phosphate are used in the pharmaceutical industry. Milled material is typically used in wet-granulated or roller-compacted formulations. The 'unmilled' or coarse-grade material is typically used in direct-compression formulations.

Dibasic calcium phosphate dihydrate is nonhygroscopic and stable at room temperature. However, under certain conditions of temperature and humidity, it can lose water of crystallization below 100°C. This has implications for certain types of packaging and aqueous film coating since the loss of water of crystallization appears to be initiated by high humidity and by implication high moisture vapor concentrations in the vicinity of the dibasic calcium phosphate dihydrate particles.⁽¹⁻⁵⁾

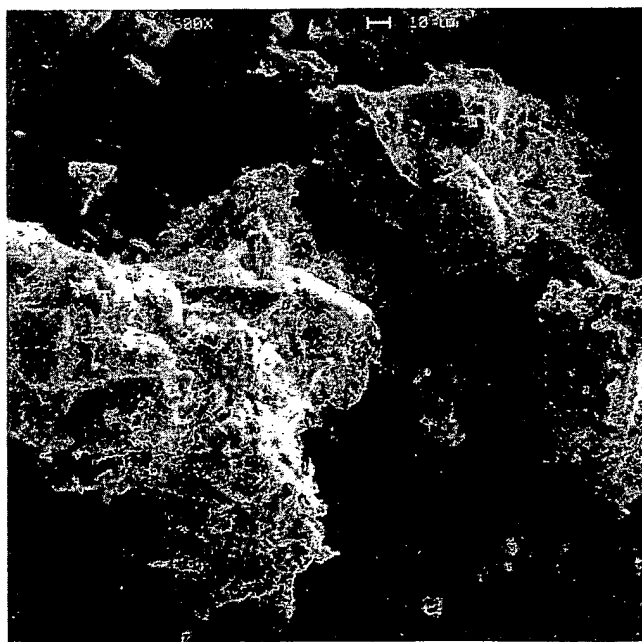
Dibasic calcium phosphate dihydrate is used in toothpaste and dentifrice formulations for its abrasive properties.

8. Description

Dibasic calcium phosphate dihydrate is a white, odorless, tasteless powder or crystalline solid. It occurs as monoclinic crystals.

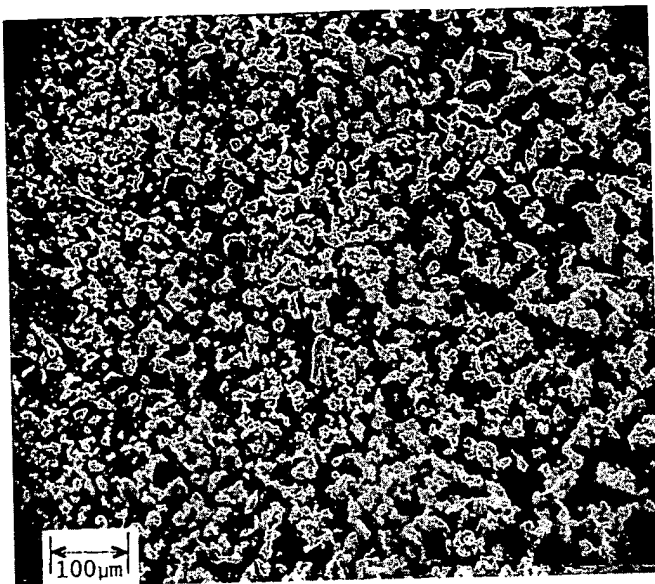
SEM: 2

Excipient: Dibasic calcium phosphate dihydrate, coarse grade
Manufacturer: Penwest Pharmaceuticals
Lot: W28C
Magnification: 300x

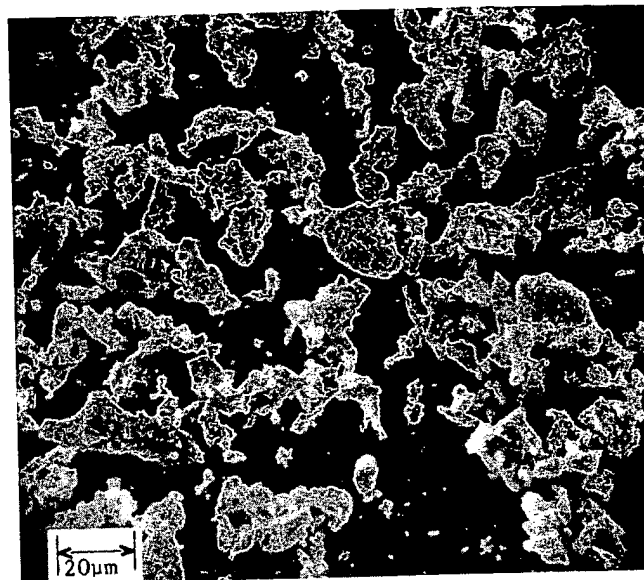


SEM: 3

Excipient: Dibasic calcium phosphate dihydrate
 Manufacturer: Stauffer Chemical Co
 Lot: 16A-1 (89)
 Magnification: 120×

**SEM: 4**

Excipient: Dibasic calcium phosphate dihydrate, coarse grade
 Manufacturer: Stauffer Chemical Co
 Lot: 16A-1 (89)
 Magnification: 600×

**9. Pharmacopeial Specifications**

Test	JP	PhEur	USP
Identification	+	+	+
Characters	—	+	—
Description and solubility	+	—	+
Loss on ignition	—	—	24.5-26.5%
Loss on drying	19.5-22.0%	—	—
Acid insoluble substances	≤ 0.05%	—	≤ 0.2%
Heavy metals	≤ 31 ppm	≤ 40 ppm	≤ 0.003%
Chloride	≤ 0.248%	≤ 330 ppm	0.25%
Fluoride	—	≤ 100 ppm	≤ 50 ppm
Sulfate	≤ 0.160%	≤ 0.5%	≤ 0.5%
Carbonate	+	+	+
Barium	+	+	+
Arsenic	≤ 2 ppm	≤ 10 ppm	≤ 3 ppm
Monocalcium and tricalcium phosphates	—	+	—
Organic volatile impurities	—	—	+
Iron	—	≤ 400 ppm	—
Assay	—	98.0-101.0%	98.0-105.0%

10. Typical Properties

Acidity/alkalinity:

pH = 7.4 (20% slurry of *DI-TAB*)

Angle of repose: 28.3° for *Emcompress*.⁽⁶⁾

Compressibility: See Figs. 1, 2, 3, and 4.^(a)

Compression pressure: 39.46 kN/cm²

Tensile strength: 0.5605 kN/cm²

Permanent deformation: 66.7 kN/cm²

Brittle fracture: 0.1014

Reduced modulus of elasticity: 7917

Density (bulk): 0.915 g/cm^{3(b)}

Density (tapped): 1.17 g/cm^{3(b)}

Density (true): 2.389 g/cm^{3(b)}

Flowability:

27.3 g/s for *DI-TAB*;

11.4 g/s for *Emcompress*.⁽⁶⁾

Melting point: decomposes below 100°C with loss of water.⁽¹⁻³⁾

Moisture content: dibasic calcium phosphate dihydrate contains two molecules of water of crystallization which can be lost at temperatures below 100°C. See also Fig. 5.^(c)

Particle size distribution:

Average particle diameter = ≈ 180 μm for *DI-TAB*;

Average particle diameter = ≈ 9 μm for fine powder.

See also Fig. 6.^(a)

Solubility: practically insoluble in ethanol, ether, and water; soluble in dilute acids.

Specific surface area: 0.44-0.46 m²/g for *Emcompress*.^(b)

^(a) Handbook of Pharmaceutical Excipients, First Edition.

^(b) Results of laboratory project for third edition.